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EXAMINER	
WONG, JENNIFER SHIN SHIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/686,619	O'TOOLE ET AL.	
	Examiner	Art Unit	
	Jennifer Wong	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 1-8, drawn to methods to detect midkine gene expression levels, classified in class 435, subclass 6.

II. Claim 9-17, drawn to pharmaceutical compositions, classified in class 514, subclass 1.

III. Claim 17, drawn to methods of administering pharmaceutical compositions, classified in 514, subclass 2.

IV. Claims 18-19, drawn to methods drawn to identify midkine agonists 4, classified in class 435, subclass 7.1.

V. Claim 20, drawn to methods to identify midkine modulators, classified in class 435, subclass 4.

VI. Claim 21, drawn to kits to diagnose lupus comprising nucleic acids, classified in class 536, subclass 23.1.

VII. Claim 21, drawn to a kit to diagnose lupus comprising antibodies, classified in class 536, subclass 387.1.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case, the pharmaceutical compositions of invention II are not required to practice the methods of invention I.

Inventions I and III are drawn to patentably distinct methods requiring the use of different reagents, involving different process steps and having different outcomes or objectives. In particular, the method of invention I require the use of a patient and control samples and involve hybridization assays in order to achieve the objective of detecting midkine gene expression levels. The methods of invention III, on the other hand, require the use of pharmaceutical compositions and mammals and involves introducing said pharmaceuticals to said mammals in order to achieve the objective of administering an effective amount of pharmaceutical compositions to prevent or treat lupus. The methods of inventions I and III are novel and unobvious over one another.

Inventions I and IV are drawn to patentably distinct methods requiring the use of different reagents, involving different process steps and having different outcomes or objectives. In particular, the method of invention I require the use of test samples, controls, and antibodies and involve hybridization assays in order to achieve the objective of detecting midkine gene expression levels. On the other hand, the methods of invention IV require labeled peptides and candidate agents able to bind to midkine, and involve hybridization assays to determine binding affinities of said candidate agent

with said labeled peptide in order to achieve the objective of identifying midkine agonists. The methods of invention I and IV are novel and unobvious over one another.

Inventions I and V are drawn to patentably distinct methods requiring the use of different reagents, involving different process steps and having different outcomes or objectives. In particular, the method of invention I require the use of test samples, controls, and antibodies and involve hybridization assays in order to achieve the objective of detecting midkine gene expression levels. The methods of invention V require the use of peptides and candidate agents capable of modulating midkine activity and involve hybridization assays and comparing said agents' activities in the presence of said peptides in order to achieve the objective of identifying midkine modulators. The methods of inventions I and V are novel and unobvious over one another.

Inventions I and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case, the nucleic acids of invention VI are not required to practice the methods of invention I.

Inventions I and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case, the antibodies of invention VII are not required to practice the methods of invention I.

Inventions II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. 806.05(h)). In the instant case, the pharmaceutical compositions of invention II can be used in a materially different process, such as for methods of treatment.

Inventions II and IV, and II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case, the pharmaceutical compositions of invention II are not required to practice the methods of invention IV and V.

Inventions II and VI are patentably distinct in structure and physicochemical properties. Invention II is drawn to pharmaceutical compositions whereas invention VI is drawn to nucleic acids. Because pharmaceuticals are composed of bioreactive agents and carriers of said agents that are capable of being administered to patients and nucleic acids are composed of nucleotides, the inventions have different structural and functional properties. Furthermore, the products are utilized in different methodologies, such that nucleic acids may be utilized in hybridization assays, while pharmaceuticals may be utilized in methods of treatment. Synthesis of the nucleic acids of invention VI do not require the particular products of the pharmaceuticals of invention II since nucleic acids can be isolated from natural sources or chemically synthesized.

Inventions II and VII are patentably distinct in structure and physicochemical properties. Invention II is drawn to pharmaceutical compositions whereas invention VII is drawn to antibodies. Pharmaceutical compositions and antibodies differ in their structure, function and effect. While the pharmaceutical compositions of invention II consist of bioreactive agents and carriers of said agents that are capable of being administered to patients, the antibodies of invention VII encompass 2 heavy chains and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 CDRs that function to bind an epitope. Pharmaceuticals and antibodies also have different functional properties and can be utilized in different methodologies, such that pharmaceuticals may be used in methods of treatment, whereas antibodies may be used in protein binding methods. Synthesis of the antibodies of inventions VII does not require the particular products of the pharmaceutical compositions of invention I since the antibodies can be isolated from natural sources or chemically synthesized.

Inventions III and IV are drawn to patentably distinct methods requiring the use of different reagents, involving different process steps and having different outcomes or objectives. In particular, the methods of invention III require the use of pharmaceutical compositions and mammals and involves introducing said pharmaceutical compositions into said mammals in order to achieve the objective of administering an effective amount of pharmaceutical compositions to prevent or treat lupus. The methods of invention IV require labeled peptides and candidate agents able to bind to midkine, and involve hybridization assays to determine binding affinities of said candidate agent with

said labeled peptide in order to achieve the objective of identifying midkine agonists. The methods of inventions III and IV are novel and unobvious over one another.

Inventions III and V are drawn to patentably distinct methods requiring the use of different reagents, involving different process steps and having different outcomes or objectives. In particular, the methods of invention III require the use of pharmaceutical compositions and mammals and involves introducing said pharmaceutical compositions in order to achieve the objective of administering an effective amount of pharmaceutical compositions to prevent or treat lupus. The methods of invention V require the use of peptides and candidate agents capable of modulating midkine activity and involve hybridization assays and comparing said agents' activities in the presence of said peptides in order to achieve the objective of identifying midkine modulators. The methods of inventions III and V are novel and unobvious over one another.

Inventions III and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, the nucleic acids of invention V are not required to practice the methods of invention III.

Inventions III and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, the antibodies of invention VII are not required to practice the methods of invention III.

Inventions IV and V are drawn to patentably distinct methods requiring the use of different reagents, involving different process steps and having different outcomes or objectives. In particular, the methods of invention IV require labeled peptides and candidate agents able to bind to midkine, and involve hybridization assays to determine binding affinities of said candidate agent with said labeled peptide in order to achieve the objective of identifying midkine agonists. The methods of invention V require the use of peptides and candidate agents capable of modulating midkine activity and involve hybridization assays and comparing said agents' activities in the presence of said peptides in order to achieve the objective of identifying midkine modulators. The methods of inventions IV and V are novel and unobvious over one another.

Inventions IV and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, the nucleic acids of invention VI are not required to practice the methods of invention IV.

Inventions IV and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, the antibodies of invention VII are not required to practice the methods of invention IV.

Inventions V and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, the nucleic acids of invention VI are not required to practice the methods of invention V.

Inventions V and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, the antibodies of invention VII are not required to practice the methods of invention V.

Inventions VI and VII are patentably distinct in structure and physicochemical properties. Invention VI is drawn to nucleic acids whereas invention VII is drawn to antibodies. The nucleic acids and antibodies differ in their structure, function and effect. While the nucleic acids of invention VI consist of nucleotides, the antibodies of invention VII encompass 2 heavy chains and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 CDRs that function to bind an epitope. The nucleic acids and antibodies also have different functional properties and can be utilized in different methodologies, such that nucleic acids may be used in hybridization methods, whereas antibodies may be used in protein binding methods. Synthesis of the antibodies of inventions VII does not require the particular products of the nucleic acids of inventions VI since the antibodies can be isolated from natural sources or chemically synthesized.

3. Further, should Applicants elect invention II, this group is subject to an additional restriction requirement as follows.

Claims 9-16 is subject to an additional restriction since this claim is not considered to recite a proper genus/Markus group.

Specifically, claims 9-16 claim pharmaceutical compositions that is an agent that modulates midkine activity or midkine gene expression. Each of these agents comprise distinct molecular and chemical compositions, and thereby has a different biological functions as one agent controls or regulates midkine activity, and another agent the either allows or does not allow midkine expression. Given the differences in structure and function, the Markush group set forth in claims 9-16 is not considered to constitute a proper genus, and therefore is subject to a further requirement. A keyword and literature search for midkine activity modulators is not co-extensive with a keyword and literature search for midkine gene expression modulators. A finding that midkine activity modulators are obvious or non-novel would not necessarily render obvious or non-novel midkine gene expression modulators. Similarly, a finding that midkine activity modulators are non-obvious or novel would not necessarily render midkine gene expression modulators as non-obvious or novel. Accordingly, a search of midkine activity modulator agents and midkine gene expression agents from claims 9-16 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and the corresponding examination of more than one of the claimed sequences. Accordingly, Applicants are required to elect either a midkine activity modulator or a midkine gene expression modulator. Note that this is not a species selection.

Additionally, claims 9-16 claim pharmaceutical compositions comprising antibodies, antisense polynucleotides, gene therapy vectors, polynucleotides capable of inhibiting midkine gene expression by RNAi, and siRNA sense or antisense polynucleotides. Each of these pharmaceutical compositions differs in their structure, function, and effect. Antisense polynucleotides, polynucleotides capable of inhibiting midkine gene expression by RNAi , and siRNA sense and antisense polynucleotides are drawn to nucleic acids and consist of nucleotides. Gene therapy vectors are drawn to proteins and are composed of amino acids. Furthermore, nucleic acids and proteins are utilized in different methodologies, such that nucleic acids may be utilized in hybridization assays, while proteins may be utilized in ligand binding assays or to generate antibodies. Although antibodies are also composed of amino acids, proteins and antibodies differ in their primary amino acid sequence and in the secondary and tertiary structures. While proteins are a single chain molecule, antibodies encompasses 2 heavy chains and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 CDRs that function to bind an epitope. Nucleic acids differ from antibodies in such that they can be utilized for the synthesis of nucleic acids and proteins. Further, a keyword and literature search of said pharmaceutical agents are not co-extensive. For instance, a search for antibodies is not co-extensive with antisense polynucleotides, gene therapy vectors, polynucleotides capable of inhibiting midkine gene expression by RNAi, and siRNA sense or antisense polynucleotides. Further, a finding that said antibodies are anticipated or obvious over the prior art would not necessarily extend to a finding that antisense polynucleotides,

gene therapy vectors, polynucleotides capable of inhibiting midkine gene expression by RNAi, and siRNA sense or antisense polynucleotides are also anticipated or obvious over the prior art. Additionally, a finding that said antibodies are novel or non-obvious over the prior art would not extend to a finding that antisense polynucleotides, gene therapy vectors, polynucleotides capable of inhibiting midkine gene expression by RNAi, and siRNA sense or antisense polynucleotides are novel or nonobvious over the prior art. The pharmaceutical compositions of claims 9-16 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and the corresponding examination of more than one of the claimed sequences. Accordingly, Applicants are required to elect either antibody, antisense polynucleotides, gene therapy vectors, polynucleotides capable of inhibiting midkine gene expression by RNAi, and siRNA sense or siRNA antisense polynucleotides as a pharmaceutical composition. Note that this is not a species selection.

Further, claim 16 reads on patentably distinct inventions drawn to multiple nucleic acid sequences comprising siRNA sense or siRNA antisense strands. The claims encompass 48 nucleic acids set forth in Table 2 and consist of distinct nucleotide sequences, and a further restriction is applied to each invention. Applicants must elect a single nucleic acid sequence to be examined.

It is noted that each of the nucleic acid sequences constitute distinct chemical compounds and each has a distinct functional property. The chemical structure of each nucleic acid sequence and of each molecule of a nucleic acid sequence is distinct from each of the other nucleic acid sequence. For example, a polynucleotide comprising

UUCUUUCUAUUCCACUUCUUC (SEQ ID NO: 7) is chemically, structurally and functionally distinct from a polynucleotide comprising AGUACAAGUUUGAGAACUGUU (SEQ ID NO: 30). Further, a search for a nucleic acid comprising UUCUUUCUAUUCCACUUCUUC (SEQ ID NO: 7) would not be co-extensive with a search for a nucleic acid comprising AGUACAAGUUUGAGAACUGUU (SEQ ID NO: 30). Additionally, a reference which renders obvious UUCUUUCUAUUCCACUUCUUC (SEQ ID NO: 7) will not necessarily also render obvious AGUACAAGUUUGAGAACUGUU (SEQ ID NO: 30). Similarly, a search indicating that UUCUUUCUAUUCCACUUCUUC (SEQ ID NO: 7) is novel or unobvious would not extend to a holding AGUACAAGUUUGAGAACUGUU (SEQ ID NO: 30) is also novel or unobvious. Accordingly, should a polynucleotide comprising siRNA sense or siRNA antisense strand be elected as a pharmaceutical composition, Applicants are required to elect a single nucleotide sequence from Table 2. Note that this is not a species selection.

In Summary, with respect to claim 9, Applicants should elect either i) an agent that modulates midkine activity or ii) an agent that modulates midkine expression. With respect to claims 11-16, Applicant should further elect either: a polypeptide, a polynucleotide, a polysaccharide, a small organic molecule, an inorganic molecule, an antibody, consistent with the election of i) or ii). If applicant elects a polynucleotide, then applicant should further elect a polynucleotide selected from the group consisting of a gene therapy polynucleotide, an siRNA polynucleotide, and a RNAi polynucleotide.

Additionally, if Applicants elect a siRNA polynucleotide, then applicants must elect one of the siRNA polynucleotides selected from the polynucleotides set forth in Table 2.

4. Further, should Applicants elect invention III, claim 11 will be rejoined with claim 17. Claim 11 is drawn towards pharmaceutical compositions, and it is grouped with invention II as it depends from claim 9. However, if Applicants intend that claim 11 is drawn towards methods of administrating of pharmaceutical compositions, it will be rejoined with invention III.

5. Claim 21 have been presented in an improper Markush format, as distinct products and distinct methods are improperly joined by the claims. Inventions VI and VII read on patentably distinct inventions drawn to multiple probes capable of hybridizing to a polynucleotide encoding the amino acid sequence of SEQ. ID. No: 1, and antibodies capable of binding to the amino acid sequence of SEQ ID. No: 1. Inventions VI and VII are patentably distinct in structure and physicochemical properties. Invention VI is drawn to nucleic acids whereas invention III is drawn to antibodies. The nucleic acids and antibodies differ in their structure, function and effect. While the nucleic acids of invention VI consist of nucleotides, the antibodies of invention VII encompass 2 heavy chains and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 CDRs that function to bind an epitope. The nucleic acids and antibodies also have different functional properties and can be utilized in different methodologies, such that nucleic acids may be used in hybridization methods, whereas antibodies may be used in protein binding methods. Given the differences in structure and function, the Markush group

set forth in claim 21 is not required to constitute a proper genus, and therefore is subject to a further restriction requirement.

6. These inventions are distinct for the reasons given above and have acquired a different status in the art as demonstrated by their different classification and recognized divergent subject matter. Further, inventions I-VII require different searches that are not co-extensive. For example, a search for the methods of inventions I and III-V are not coextensive with one another. A keyword and literature search of the methods to detect midkine gene expression levels of invention I would not be coextensive the methods of administering the pharmaceuticals of invention III, methods of identifying midkine agonists of invention IV, or the methods to identify midkine modulators of invention V. Further, a finding that invention I is anticipated or obvious over the prior art would not necessarily extend to a finding that the methods of III-V are anticipated or obvious over the prior art. Similarly, a finding that invention I is novel and unobvious over the prior art would not necessarily extend to a finding that the methods of III-V are novel or unobvious over the prior art. Additionally, inventions II and VI-VII require different searches that are not coextensive. For instance, a keyword and literature search for the pharmaceutical compositions of invention II are not coextensive with the nucleic acids of invention VI or the antibodies of invention VII. Further, a finding that the pharmaceutical compositions of invention II is anticipated or obvious over the prior art would not necessarily extend to a finding that the nucleic acids of invention VI or the antibodies of invention VII are anticipated or obvious over the prior art. Similarly, a finding that pharmaceutical compositions of invention II is novel and unobvious over the prior art

would not necessarily extend to a finding that the nucleic acids of invention VI or the antibodies of invention VII are novel or unobvious over the prior art. Accordingly, examination of these distinct inventions would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper.

7. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

9. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Wong whose telephone number is (571) 272-1120. The examiner can normally be reached on Monday-Friday; 8 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer Wong

CARLA J. MYERS
PRIMARY EXAMINER